Doc Code: AP.PRE.REQ

PTO/SB/33 (07-05)
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PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) 1781-0215P	
	Application Number 09/766,412-Conf. #7335	Filed January 22, 2001
	First Named Inventor Ruowen GE et al.	
	Art Unit 1654	Examiner A. A. Mohamed

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant /inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)

☒ attorney or agent of record.
Registration number 36,623

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34. _____

Signature

Mark J. Nuell
Typed or printed name

(703) 205-8043
Telephone number

January 16, 2007
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of 1 forms are submitted.

Docket No.: 1781-0215P
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Ruowen GE, et al.

Application No.: 09/766,412

Confirmation No.: 7335

Filed: January 22, 2001

Art Unit: 1654

For: SMALL PEPTIDES HAVING ANTI-ANGIOGENIC AND ENDOTHELIAL CELL INHIBITION ACTIVITY

Examiner: A. A. MOHAMED

DOCUMENT IN SUPPORT OF
REQUEST FOR PRE-APPEAL BRIEF CONFERENCE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir

Claims 10, 15, 16, and 20 were rejected under the first paragraph of 35 U.S.C. §112 as allegedly failing to comply with the written description requirement. Each of claims 10, 15, 16, and 20 (as well as each of non-rejected claims 25, 26, and 27, and "withdrawn" claims 30, 31, and 32) relates to one or more ***specific*** sequences. It is not clear how the rejection stated by the Examiner on pages 2-8 of the Office Action applies to claims 10, 15, 16, and 20.

Claims 1, 2, 6-8, 13, 14, 19, and 29 were rejected under the first paragraph of 35 U.S.C. §112 as allegedly failing to comply with the written description requirement.

There is a strong presumption that an adequate written description of the claimed invention is present when an application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why ***persons skilled in the art*** would not recognize in the disclosure a description of the invention defined by the claims") (emphasis supplied).

In addition to its biological recitations, claim 1 herein recites a peptide that comprises "a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide". Endostatin is a well known polypeptide of 184 amino acids. There are only a finite number of 7-amino acid portions of the endostatin peptide.

A ***person skilled in the art***, upon reading the present specification, could readily envision the list of all the recited 7-20 amino acid "portions" of endostatin. A ***person skilled in the art,*** based upon the teachings in the specification, would learn what portion of the endostatin polypeptide should be obtained and would readily envision how to eliminate from the 'all 7-20 amino acid portions' list all portions that did not contain a pair of proline residues, at least one of which is at or penultimate to a terminus of the peptide "portion" of the 184 amino acid endostatin sequence. These two simple manipulations of the endostatin sequence, each of which is within the expected skill of the art, would leave the small group of proline-pair peptides that represent structures within claim 1.

To determine which of those structures is actually encompassed by claim 1, the ***person skilled in the art*** would then run tests that are described in the present specification on each of the peptides, in the

small group of proline-pair peptides that had been derived from the endostatin sequence, in order to determine whether each peptide exhibits an IC_{50} of 20 μM or less in a bovine aorta endothelial cell proliferation assay or exhibits inhibition of angiogenesis in a chick chorioallantoic membrane assay of at least 30% at a dose of 50 μg/coverslip.

These steps – which once conceived and described as in the present specification are technologically simple – would identify each and every peptide covered by claim 1. Applicants contend that there is nothing in these steps that is beyond the expected skill of those persons to whom the present disclosure is directed. The present disclosure provides ***persons skilled in the art*** with a written description of the claimed invention.

In the paragraph bridging pages 4-5 of the Office Action, the Examiner alleges that "claims 1, 7 and 10 encompass all the fragments cited above". What fragments are "cited above"? Where?

In the paragraph bridging pages 4-5 of the Office Action, the Examiner alleges that "There is no written description indicating the claimed fragments for the peptide ... except for the elected invention of the peptide having the amino acid sequences [sic] of SEQ ID NO:30". This allegation ignores the amino acid sequences of SEQ ID NO:29, SEQ ID NO:31, and SEQ ID NO:32. In any event, as noted above, claim 1 starts with a known moiety – endostatin. Then claim 1 takes a portion of that known moiety, not just any portion, but a portion having at least 7 and at most 20 amino acids. But not all 7-20 amino acid portions of endostatin are covered by claim 1. Only those that both contain a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide and exhibit an IC_{50} of 20 μM or less in a bovine aorta endothelial cell proliferation assay or exhibits inhibition of angiogenesis in a chick chorioallantoic membrane assay of at least 30% at a dose of 50 μg/coverslip. So claim 1 starts with a known group of peptides – all of which are encompassed by

endostatin – and claim 1 selectively reduces that group by both structural considerations and separate biological considerations, to arrive at a clearly defined, selected subgroup of the original known starting group of peptides. All of the above is described in the specification, for instance, from line 22 on page 6 through line 18 on page 7.

In the full paragraph on page 5 of the Office Action, the Examiner alleges that "Applicant contemplates ***modification*** of a portion of an endostation protein by substitution from 0 to 20 of amino acid residues in the peptide". Emphasis supplied. Relevant language in claim 1 is as follows: "A peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide". The Examiner is requested to point out where that claim language refers to substitution of amino acids.

In the paragraph bridging pages 5-6 of the Office Action, the Examiner argues that "Applicant is attempting to extrapolate to a broad diversity of a portion of an endostatin protein ...by claiming the substitution of any amino acid residue having less than 20 amino acids in length". It is apparent that the Examiner's 'written description' rejection is based upon a misunderstanding of the claims. Not one of the rejected claims refers to substitution.

Also in the paragraph bridging pages 5-6 of the Office Action, the Examiner argues that "in claim 1, any number of amino acids (at least from 0 to 20) can be replaced with any number ranging from 7-20 conservative or non-conservative amino acid residues". It is not clear what aspect of the claim 1 language (with emphasis supplied) "peptide comprising ***a portion of an endostatin protein***, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide" the

Examiner relies upon as basis for this assertion that claim 1 includes replacing one or more amino acids in the endostatin portion with at least 7 non-conservative amino acid residues.

The Examiner has not rebutted the strong presumption that an adequate written description of the inventions of each of claims 10, 15, 16, or 20 – and of the inventions of each of claims 1, 2, 6-8, 13, 14, 19, and 29 – was present when the application is filed. *In re Wertheim, supra.* Withdrawal of the rejection of claims herein under the first paragraph of 35 U.S.C. §112 as allegedly failing to comply with the written description requirement – at least as the rejection is stated in the Final Rejection of 10/16/2006 – is in order and is earnestly solicited.

If there are any questions concerning this application, the Examiner is invited to telephone Richard Gallagher (Reg. No. 28,781) at (703) 205-8008.

Dated: January 16, 2007

Respectfully submitted,

By _____
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